Long-Term Outcomes of Secondary Atrial Fibrillation in the Community

The Framingham Heart Study

Steven A. Lubitz, MD, MPH*; Xiaoyan Yin, PhD*; Michiel Rienstra, MD, PhD*; Renate B. Schnabel, MD, MSc; Allan J. Walkey, MD, MSc; Jared W. Magnani, MD, MSc; Faisal Rahman, MD; David D. McManus, MD, MSc; Thomas M. Tadros, MD; Daniel Levy, MD; Ramachandran S. Vasan, MD; Martin G. Larson, ScD; Patrick T. Ellinor, MD, PhD; Emelia J. Benjamin, MD, ScM

Background—Guidelines have proposed that atrial fibrillation (AF) can occur as an isolated event, particularly when precipitated by a secondary, or reversible, condition. However, knowledge of long-term AF outcomes after diagnosis during a secondary precipitant is limited.

Methods and Results—In 1409 Framingham Heart Study participants with new-onset AF, we examined associations between first-detected AF episodes occurring with and without a secondary precipitant and both long-term AF recurrence and morbidity. We selected secondary precipitants based on guidelines (surgery, infection, acute myocardial infarction, thyrotoxicosis, acute alcohol consumption, acute pericardial disease, pulmonary embolism, or other acute pulmonary disease). Among 439 patients (31%) with AF diagnosed during a secondary precipitant, cardiothoracic surgery (n=131 [30%]), infection (n=102 [23%]), noncardiothoracic surgery (n=87 [20%]), and acute myocardial infarction (n=78 [18%]) were most common. AF recurred in 544 of 846 eligible individuals without permanent AF (5-, 10-, and 15-year recurrences of 42%, 56%, and 62% with versus 59%, 69%, and 71% without secondary precipitants; multivariable-adjusted hazard ratio, 0.65 [95% confidence interval, 0.54–0.78]). Stroke risk (n=209/1262 at risk; hazard ratio, 1.13 [95% confidence interval, 0.82–1.57]) and mortality (n=1098/1409 at risk; hazard ratio, 1.00 [95% confidence interval, 0.87–1.15]) were similar between those with and without secondary precipitants, although heart failure risk was reduced (n=294/1107 at risk; hazard ratio, 0.74 [95% confidence interval, 0.56–0.97]).

Conclusions—AF recurs in most individuals, including those diagnosed with secondary precipitants. Long-term AF-related stroke and mortality risks were similar between individuals with and without secondary AF precipitants. Future studies may determine whether increased arrhythmia surveillance or adherence to general AF management principles in patients with reversible AF precipitants will reduce morbidity. **(*Circulation*. 2015;131:1648-1655. DOI: 10.1161/CIRCULATIONAHA.114.014058.)**

Key Words: atrial fibrillation ■ atrial flutter ■ epidemiology ■ heart failure ■ risk factors ■ stroke

There is widespread recognition that atrial fibrillation (AF) may recur episodically or be present in a sustained fashion after a first-detected episode, yet there exists a prevailing assumption that AF may occur as an isolated event without recurrence, particularly when an acute reversible, or secondary, precipitant is associated with the episode. Previous consensus guidelines stated that treatment of an underlying reversible precipitant may "terminate the arrhythmia without recurrence,"[1] although, as acknowledged in more recent guidelines, data addressing the long-term follow-up of such patients are incomplete.[2]

Clinical Perspective on p 1655

Received August 15, 2014; accepted March 10, 2015.

From Cardiovascular Research Center (S.A.L., P.T.E.) and Cardiac Arrhythmia Service (S.A.L., P.T.E.), Massachusetts General Hospital, Boston; Boston University and National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, MA (X.Y., J.W.M., D.L., R.S.V., M.G.L., E.J.B.); Department of Cardiology, University of Groningen, University Medical Center Groningen, The Netherlands (M.R.); Department of General and Interventional Cardiology, University Medical Center Hamburg Eppendorf, Hamburg, Germany (R.B.S.); Pulmonary Center and Section of Pulmonary and Critical Care Medicine (A.J.W.), Section of Cardiovascular Medicine (J.W.M., R.S.V., E.J.B.), and Section of Preventive Medicine (R.S.V., E.J.B.), Department of Medicine, Boston University School of Medicine, MA; Department of Medicine, Boston University Medical Center, MA (F.R.); Departments of Medicine and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester (D.D.M.); Sutter Medical Group, Sacramento, CA (T.M.T.); Population Sciences Branch, National Heart, Lung, and Blood Institute, Bethesda, MD (D.L.); Department of Mathematics and Statistics, Boston University, MA (M.G.L.); and Departments of Biostatistics (M.G.L.) and Epidemiology (E.J.B., R.S.V.), Boston University School of Public Health, MA.

Guest Editor for this article was Matthew A. Allison, MD.

*Drs Lubitz, Yin, and Rienstra contributed equally to this work.

The online-only Data Supplement is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.114.014058/-/DC1.

Correspondence to Steven A. Lubitz, MD, MPH, Cardiac Arrhythmia Service and Cardiovascular Research Center, Massachusetts General Hospital, 55 Fruit St, GRB 109, Boston, MA 02114. E-mail slubitz@mgh.harvard.edu

There is a need to understand the long-term clinical implications of AF that occur in the context of secondary precipitants. The distinction as to whether AF is likely to recur after a particular precipitant has important clinical implications, because it may affect whether AF is regarded as a chronic condition and thus whether risks of heart failure, stroke, and increased mortality typically attributed to AF are applicable to a specific patient. Perceptions about the likelihood of AF recurrence may influence how closely patients are monitored for recurrence and whether general principles of AF management, such as thromboembolism prophylaxis, are recommended. Therefore, we sought to determine whether the long-term risks of both AF recurrence and morbidity differ according to the presence or absence of potential secondary AF precipitants in community-dwelling individuals from the Framingham Heart Study.

Methods

Participants

Participants from the Framingham Heart Study original[3] and offspring[4] cohorts with first-detected AF between 1949 and 2012 were eligible for this study (n=1782). We excluded individuals who died within 30 days of first-detected AF (n=215) in keeping with previous analyses,[5,6] because we believed that events occurring during this interval might plausibly be related to the index AF event and because our aim was to assess the relations between the presence or absence of secondary AF precipitants and long-term clinical outcomes. We also excluded individuals with incomplete baseline covariate data (n=158). A total of 1409 individuals remained eligible for analysis. The Boston University Medical Center Institutional Review Board approved the study protocols, and all of the participants signed consent forms at each examination cycle.

Assessment of First-Detected AF

At each Framingham Heart Study clinic examination (approximately every 2 years for the original cohort and every 4 to 8 years for the offspring cohort), participant medical histories, physical examinations, and ECGs were obtained to assess symptoms and findings suggestive of cardiovascular disease. Records of all interim outpatient appointments and hospitalizations for cardiovascular disease were sought for manual review by mailings and telephone calls via health history updates every 24 months. Participants were classified as having AF if the arrhythmia was present on an ECG obtained at a Framingham Heart Study clinic visit or encounter with an external clinician, Holter monitoring, or noted in hospital records, as described previously.[7,8]

Study investigators reviewed all of the available records, regardless of symptoms, to determine the dates of AF. During ascertainment of each first-detected AF episode, clinical records were reviewed and a standardized form was completed to capture potential precipitants of the first-detected episode. Two physicians adjudicated first-detected AF events and precipitants, and at least 1 cardiologist adjudicated subsequent encounters (see below).

Definition of Secondary AF

We defined precipitants of the initial AF event as secondary if the adjudicated precipitant included a potentially reversible factor, as outlined in American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines.[1,2] Secondary precipitants included surgery (within 30 days, which we subdivided into cardiothoracic and noncardiothoracic), acute myocardial infarction (within 30 days), acute infection (including but not restricted to sepsis, nonpulmonary infections, pneumonia, bronchitis, and chronic obstructive lung disease exacerbation), acute alcohol consumption, thyrotoxicosis, acute pericardial disease (pericarditis or tamponade), acute pulmonary embolism, and other acute pulmonary pathology (eg, pneumothorax and bronchoscopy related). If individuals had more than 1 precipitant, we designated a main precipitant in a hierarchical fashion using the following sequence: cardiothoracic surgery, noncardiothoracic surgery, acute myocardial infarction, acute infection, and other precipitants.

Ascertainment of Covariates, Recurrent AF, Heart Failure, Stroke, and Death

Baseline characteristics were ascertained from study examinations, with the exception of AF precipitant, age, and medical therapy associated with the first-detected episode. We included characteristics from the closest examination within 10 years before first-detected AF (median, 1.56 years [25th percentile, 0.54; 75th percentile, 3.32]). Treatment with antiarrhythmic medications, antiplatelet agents, and anticoagulants was ascertained at the first-detected AF episode and each subsequent physician encounter with a cardiac rhythm assessment.

After first-detected AF, we reviewed subsequent study visits and external healthcare encounters (outpatient and hospital) for evidence of AF. If the cardiac rhythm remained stable during a hospitalization, only 1 ECG was coded. If the rhythm varied during a hospitalization, the first episode of AF, first episode of sinus rhythm, and final cardiac rhythm were recorded. We classified cardioversion attempts as unsuccessful when AF was noted within 24 hours of the cardioversion attempt or when it was described as unsuccessful in the medical chart. Otherwise, we classified cardioversions as successful. A panel of 3 study investigators adjudicated strokes and heart failure events using published criteria.[9] For strokes (including ischemic or hemorrhagic cerebral infarctions), the panel included a neurologist. Additional details regarding data ascertainment are in the online-only Data Supplement. Participants in our analysis were followed through 2012, to their last examination, health history update, or death.

Derivation of Clinical Outcome Risk Pools

Because we excluded individuals with an outcome condition present at AF onset, the number of individuals at risk for each clinical outcome varied (AF recurrence, heart failure, stroke, and mortality; Figure I in the online-only Data Supplement). For analyses of recurrent AF, we omitted individuals in a hierarchical fashion as follows: 1) those with sustained (permanent) AF (n=396) because they were not at risk for AF recurrence (defined as AF without any intercurrent sinus rhythm or successful cardioversion after first-detected AF), 2) those with only 1 ECG (n=88) or <30 days between the first and last ECG (n=45) in whom we were unable to assess for long-term AF recurrence, and 3) those who died or were last contacted within 30 days of sinus rhythm after initial AF (n=34) to ensure that restoration of sinus rhythm and a potential subsequent recurrence of AF were not associated with a terminal illness. For analyses of incident heart failure and stroke, we omitted individuals with a history of the respective conditions at or within 30 days of first-detected AF (n=302 for heart failure and n=147 for stroke).

Statistical Analysis

After first-detected AF, we estimated the cumulative incidence of AF recurrence, heart failure, stroke, or death using the Kaplan-Meier method. AF recurrence was defined as the first recurrent AF episode. We adjusted for the competing risk of death for analyses of AF recurrence, heart failure, and stroke.[10] We stratified estimates by the presence or absence of secondary AF precipitants. For analyses of heart failure, stroke, and death, person-time began 30 days after first-detected AF. For analyses of AF recurrence, person-time began 30 days after the first documented sinus rhythm (including successful cardioversion) after first-detected AF and ended at the first recurrent AF episode. Follow-up was censored at last contact for all of the analyses, as well as at death for analyses of AF recurrence, heart failure, and stroke. We assessed the multivariable-adjusted relations between secondary AF and each outcome using proportional hazards regression from which we report the hazard ratio (HR) and 95% confidence

interval (CI). We adjusted for covariates associated with AF, including age, sex, height, weight, systolic and diastolic blood pressure, treatment with antihypertensive medication, current smoking, diabetes mellitus, previous myocardial infarction, previous heart failure, and valvular heart disease.[11,12] To account for potential secular differences in AF detection, comorbidities, and treatments, we also adjusted for calendar year of AF detection and Framingham cohort (original or offspring). In additional models, we adjusted for baseline cardioversions (occurring before the beginning of person-time) and antiarrhythmic drug therapy during follow-up as a time-varying covariate. In analyses of stroke and mortality, we also adjusted for antiplatelet and anticoagulant use as time-varying covariates. Proportional hazards assumptions were verified with multiplicative interaction terms between covariates and the natural logarithm of follow-up time.

In addition, we estimated the cumulative incidence of recurrent AF according to the secondary AF precipitant categories outlined above. We compared cumulative incidences of recurrent AF across categories using the Gray test[13] and examined multivariable-adjusted relations using proportional hazards regression with cardiothoracic surgery as the referent precipitant.

Secondary Analyses

In secondary analyses we explored the associations between various factors and recurrent AF among participants with secondary precipitants using multivariable proportional hazards regression. In sensitivity analyses, we included individuals with atrial flutter (n=121; see the online-only Data Supplement for ascertainment details).

For all of the analyses, the *a priori* significance threshold was $P<0.05$ using 2-sided tests. Analyses were conducted using SAS version 9.3 for Windows (SAS Institute, Cary, NC).

Results

Among the 1409 participants with first-detected AF eligible for analysis, the mean±SD age was 74±11 years, 681 (48%) were women, and 439 (31%) had at least 1 secondary AF precipitant (Table 1). Among participants with a secondary precipitant, 294 (67%) had 1 and 145 (33%) had at least 2 precipitants (Table I in the online-only Data Supplement). Recent cardiothoracic surgery (n=131 [30%]), acute infection (n=102 [23%]), noncardiothoracic surgery (n=87 [20%]), and acute myocardial infarction (n=78 [18%]) were the most common secondary precipitants. The median (25^{th}, 75^{th} percentiles) follow-up among the 1409 participants in the analysis was 5.4 (2.3, 10.1) years. During follow-up, the median number of ECGs per person-year after first-detected AF was 0.6 (0.3, 1.5) in individuals with a secondary precipitant and 0.9 (0.5, 1.8) in those without.

Among the 846 individuals without permanent AF who were eligible for analyses of AF recurrence, 325 (38%) had a first-detected AF episode attributed to a secondary precipitant. Recurrent AF occurred in 544 individuals. The 5-, 10-, and 15-year cumulative incidences of recurrent AF were 42%, 56%, and 62% among participants with a secondary AF precipitant, in contrast to 59%, 69%, and 71% among participants without a secondary AF precipitant (Figure 1). In individuals with recurrent AF, 323 (59%) of the recurrences occurred within 2.5 years of the first-detected AF episode. Secondary AF precipitants were associated with a reduced risk of AF recurrence compared with nonsecondary AF, and the magnitude of association was not substantively altered by adjustment for clinical AF risk factors, cardioversion at baseline, or time-varying antiarrhythmic drug use (multivariable-adjusted HR, 0.65 [95% CI, 0.54–0.78]; $P<0.0001$; Table 2).

To explore whether the risk of recurrent AF varied with different secondary AF precipitants, we classified the 325 participants with a secondary precipitant eligible for AF recurrence analyses into the following categories: cardiothoracic surgery (n=118 [36%]), noncardiothoracic surgery (n=69 [21%]), acute myocardial infarction (n=56 [17%]), acute infection (n=54 [17%]), and other (n=28 [9%]). The crude proportions of AF recurrence ranged from 47% to 68% across the secondary AF precipitant subgroups. Relative to cardiothoracic surgery, other secondary precipitants were associated with a 2-fold increased hazard for recurrent AF (HR, 1.99 [95% CI, 1.41–2.79]; $P<0.001$; Table 3). Additional factors associated with recurrent AF in these models included having higher age at AF onset, weight, and valvular heart disease (Table II in the online-only Data Supplement).

During follow-up, incident heart failure occurred in 294 (27%) of 1107 individuals at risk, incident strokes in 209 (17%) of 1262 at risk, and death in 1098 (78%) of 1409 participants included in the analysis (Table 2). Approximately one-third of individuals in each of the risk pools for heart failure, stroke, and mortality had a secondary AF precipitant. The cumulative incidences of heart failure, stroke, and death are displayed in Figure 2. In multivariable models adjusted for clinical risk factors, cardioversions, and antiarrhythmic drug use, we observed a significantly reduced risk of incident heart failure among individuals with a secondary AF precipitant relative to those without (HR, 0.74 [95% CI, 0.56–0.97]; $P=0.03$). We did not observe an association between secondary AF precipitants and the risk of stroke (HR, 1.13 [95% CI, 0.82–1.57]; $P=0.45$) or death (HR, 1.09 [95% CI, 0.79–1.50]; P=0.79) or death (HR, 1.00 [95% CI, 0.87–1.15]; P=0.98; Table 2) in multivariable-adjusted models in which we additionally adjusted for antithrombotic drug use.

In addition to the 1409 individuals included in our analysis, 121 (7.9%) presented with atrial flutter as their initial rhythm (Table III in the online-only Data Supplement), of which 51 (42%) occurred in the setting of a secondary precipitant. In a sensitivity analysis, we included participants with atrial flutter and tested the associations between secondary AF precipitants and clinical outcomes (Table IV in the online-only Data Supplement). The observed associations between secondary AF precipitants and AF or flutter recurrence, heart failure, stroke, and mortality did not differ substantively from those in the sample of participants with AF alone.

Discussion

In our community-based study, approximately one-third of all incident AF cases were associated with a secondary, or potentially reversible, AF precipitant. The most common secondary precipitants were surgery, acute infection, and myocardial infarction. Although the risk of AF recurrence was greater among individuals without a secondary precipitant, nearly two-thirds of individuals in whom initial AF was attributed to a secondary precipitant had recurrent AF within 15 years. The associations between secondary precipitants and recurrent AF were robust to adjustment for a number of widely accepted AF risk factors, including valvular heart disease. Despite a lower risk for AF recurrence, long-term risks of stroke and mortality were similar between those with and without secondary AF precipitants. The risk of incident heart failure was reduced

Table 1. Characteristics of 1409 Framingham Heart Study participants in the analysis.

Characteristic	Secondary AF Precipitant	
	Absent (N=970)	Present (N=439)
Age at initial AF, y	74.3±11.3	73.3±11.0
Women	496 (51)	185 (42)
Height, cm	165±11	165±11
Weight, kg	76±18	76±17
Systolic blood pressure, mm Hg	143±24	141±23
Diastolic blood pressure, mm Hg	75±13	74±12
Antihypertensive therapy	515 (53)	235 (53)
Cigarette smoking	116 (12)	92 (21)
Diabetes mellitus	141 (15)	81 (18)
Valvular heart disease	140 (14)	48 (11)
History of heart failure	203 (21)	99 (23)
History of myocardial infarction	103 (11)	147 (33)
History of stroke	103 (11)	44 (10)
Cardioversion at first-detected AF	161 (17)	139 (32)
Antiarrhythmic drug use at baseline*	255 (26)	184 (42)
Antithrombotic drug use at baseline*†		
Any	507 (52)	191 (44)
Anticoagulant	279 (29)	107 (24)
Secondary AF precipitant‡		
Cardiothoracic surgery	–	131 (30)
Noncardiothoracic surgery		87 (20)
Acute infection§		102 (23)
Acute myocardial infarction	–	78 (18)
Other		
Pericarditis or tamponade	–	12 (3)
Thyrotoxicosis		11 (3)
Alcohol intoxication		10 (2)
Acute pulmonary embolism	–	6 (1)
Other acute pulmonary process¶	–	2 (<1)

Data are displayed as mean±SD or number (%). AF indicates atrial fibrillation.

*Data refer to the use after AF detection but before the onset of calculated person-time.

†These were defined as an antiplatelet agent (aspirin or thienopyridine) or an anticoagulant (vitamin K antagonist, factor Xa inhibitor, or thrombin inhibitor). Data were missing for 84 (6%) of participants.

‡The main precipitant is displayed (see text).

§Pneumonia or bronchitis (n=39) composed 38% of the acute infectious precipitants.

¶Data include pneumothorax (n=1), and procedure-related (bronchoscopy; n=1).

by ≈25% among individuals with a secondary AF precipitant after multivariable adjustment.

Larger series examining the longitudinal course of AF have often excluded individuals with secondary AF precipitants, limiting our understanding of the long-term course of AF in these contexts. Our observation that approximately one-third of first-detected AF episodes were associated with a secondary precipitant is supported by the substantial proportions of individuals with first-detected AF attributed to cardiac surgery,[14] thyroid disease,[14,15] and acute myocardial infarction[16] observed in other series.

There has been longstanding recognition that AF may recur after an initial episode, although reported recurrence rates have varied widely. Previous estimates of AF recurrence range from 22% to 49% within the first 3 years of detection[17–20] to >60% at 5 years of follow-up.[14] Substantial variability in AF recurrence rates in these and other reports[14,15,17–27] likely reflects heterogeneity in the sample populations, frequency of cardiac rhythm assessments, and durations of follow-up.[28] Our community-based findings are consistent with high long-term risks of AF recurrence reported previously.

Our findings support the high AF recurrence rates associated with specific secondary AF precipitants reported in several studies with shorter follow-up. Some,[29,30] but not all,[31–33] series have reported that AF after cardiac surgery is associated with an increased risk of subsequent AF. In a single-center report of 88 individuals with incident AF in the context of non-ST segment elevation myocardial infarction, 38% had recurrent AF at an average of 21 months of follow-up.[34] A recent study using Medicare claims data reported that AF recurred in 55% of individuals with new-onset AF in the context of sepsis at 5 years.[35] In a single-center study of 58 individuals with thyrotoxicosis-associated AF, 59% had recurrent AF at an average of 24 months of follow-up,[36] whereas a separate retrospective series of 106 patients reported that 38% had recurrent AF at ≈7 years of follow-up.[37] Similarly, substantial rates of AF recurrence were observed in association with new-onset AF attributed to alcohol consumption, irrespective of alcohol abuse during follow-up.[38]

Our study has 3 major implications. First, our data suggest that AF occurring in acute care settings is an indicator of increased future AF risk. Indeed, we observed that recurrent AF was frequent across common secondary precipitant subgroups, despite a lower average risk of AF recurrence among individuals with a secondary precipitant as compared with those without. These findings support aforementioned studies of secondary AF precipitants[29,30,33–38] and imply that increased vigilance for recurrent AF may be warranted in patients with a first-detected AF episode associated with a secondary AF precipitant. Reversing an acute AF precipitant may not dependably protect against long-term AF recurrence.

Second, our observations suggest that AF episodes, irrespective of the precipitant, often serve as markers of elevated risk for long-term stroke and mortality. Previous reports have indicated that new-onset AF occurring with myocardial infarction,[39] sepsis,[40] or cardiac surgery[41,42] is associated with increased morbidity relative to individuals without AF in these settings. Our findings extend these observations by demonstrating that long-term risks of stroke and mortality in individuals with new-onset AF were similar regardless of the AF precipitant, although we did observe a lower risk of heart failure in those with a secondary AF precipitant. The fact that stroke and mortality occurred with a similar incidence despite a slightly lower risk of recurrent AF in individuals with secondary precipitants may be explained by the potential underestimation of recurrent AF in the secondary AF group, differences in specific preventive therapies, lack of causality between AF and the clinical event, or lack of causality between the secondary precipitant and AF.

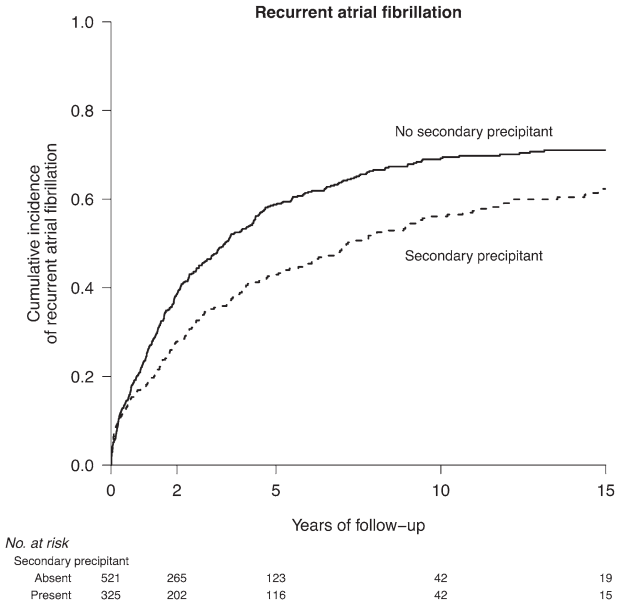

Figure 1. Risk of recurrent atrial fibrillation by presence or absence of secondary atrial fibrillation precipitants. Cumulative incidence estimates were adjusted for the competing risk of death.

Third, the substantial long-term risk of recurrent AF in individuals with secondary AF precipitants suggests that individuals with incident AF in the context of an acute precipitant may have an underlying predisposition to the arrhythmia. A two-hit hypothesis for AF is supported by an observation that several common genetic variants associated with AF in the general population were associated with an increased risk of AF in the postoperative period after cardiothoracic surgery.[43] It is alternatively possible that the high risk of recurrent AF after an initial episode reflects the propensity for the heart to sustain AF in the future, perhaps because of remodeling that occurs with AF[44] or persistent effects of the acute trigger that may not fully reverse. Future studies are warranted to determine whether predisposition to AF differs between individuals with AF in the context of secondary precipitants and those without.

Evidence-based guidelines are lacking with respect to the management of patients with AF occurring in the context of secondary precipitants. For example, the American College of Chest Physicians proposes discontinuation of anticoagulation after 30 days of sinus rhythm in patients with postoperative AF after cardiac surgery if AF is believed to be unlikely to recur, although no metrics are proposed to determine the likelihood of AF persistence or recurrence in this population.[45] In aggregate, our findings imply that AF occurring in the context of a secondary precipitant should not be dismissed and that increased vigilance is warranted given the likelihood of AF recurrence.

Presently, the optimal surveillance and thromboembolism prophylaxis strategies in patients with secondary AF remain unclear. Although existing and future health technologies such as cardiac rhythm monitoring devices may ultimately be resource effective for AF detection and prevention of AF-related morbidity, we advocate for prospective examination of such strategies. In the meantime, we submit that it is reasonable for patients to be educated regarding potential signs of AF, such as taking one's pulse, which data support as effective for AF detection.[46,47]

Our study has several strengths that distinguish it from previous reports. The study sample is composed of community-dwelling individuals, and data collection was based on standardized follow-up and routine encounters with healthcare providers. Encounters were systematically reviewed for evidence of AF, stroke, and heart failure. Our study included long-term follow-up after first-detected AF, which enabled us to study the life course of the arrhythmia. We selected AF precipitants *a priori*. We accounted for the competing risks of death when estimating the risks of AF recurrence, heart failure, and stroke so as not to overestimate cumulative incidences. We fit several multivariable models adjusting for a range of well-established risk factors for each clinical outcome, given the potential multifactorial etiology of AF, as well as each outcome.

Our study should be interpreted in the context of the observational study design. It is possible that our ascertainment of

Table 2. Risk of Clinical Events Comparing Individuals With and Without a Secondary Atrial Fibrillation Precipitant

Variable	Recurrent Atrial Fibrillation		Incident Heart Failure		Incident Stroke		Mortality	
No. of events/No. at risk	544/846		294/1107		209/1262		1098/1409	
Secondary precipitant, n (%)	325 (38)		340 (31)		395 (31)		439 (31)	
Model (referent group is atrial fibrillation without a secondary precipitant)	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age, sex, and cohort	0.70 (0.58–0.83)	<0.0001	0.97 (0.75–1.25)	0.81	1.09 (0.80–1.48)	0.57	1.08 (0.95–1.24)	0.22
Clinical atrial fibrillation risk factors*	0.70 (0.58–0.85)	0.0002	0.79 (0.60–1.04)	0.09	1.10 (0.80–1.52)	0.56	0.99 (0.86–1.14)	0.67
Clinical atrial fibrillation risk factors, baseline cardioversion, and time-varying antiarrhythmic drug use*	0.65 (0.54–0.78)	<0.0001	0.74 (0.56–0.97)	0.03	1.13 (0.82–1.57)	0.45	1.01 (0.87–1.16)	0.95
Clinical atrial fibrillation risk factors, baseline cardioversion, and time-varying antiarrhythmic, antiplatelet, and anticoagulant drug use*	–	–	–	–	1.09 (0.79–1.50)	0.79	1.00 (0.87–1.15)	0.98

CI indicates confidence interval; and HR, hazard ratio.

*Data include the age at initial atrial fibrillation, sex, cohort, year of first-detected atrial fibrillation, current smoking status, height, weight, hypertension treatment, systolic blood pressure, diastolic blood pressure, diabetes mellitus, valvular heart disease, prevalent myocardial infarction, and prevalent heart failure (in analyses of stroke and death).

Table 3. Secondary Atrial Fibrillation Precipitants in Individuals at Risk for Recurrent Atrial Fibrillation

Secondary precipitant	N	Recurrent Atrial Fibrillation, n (%)	HR (95% CI)	*P* Value
Recent cardiothoracic surgery	118	56 (47)	Referent	–
Recent noncardiothoracic surgery	69	44 (64)	1.97 (1.27–3.05)	0.002
Acute myocardial infarction	56	36 (64)	2.16 (1.33–3.50)	0.002
Acute infection	54	33 (61)	1.64 (1.00–2.70)	0.05
Other	28	19 (68)	2.42 (1.32–4.43)	0.004
All precipitants, relative to cardiothoracic surgery	207	132 (64)	1.99 (1.41–2.79)	<0.001

Data were adjusted for age at initial atrial fibrillation, sex, cohort, year of first-detected atrial fibrillation, current smoking status, height, weight, hypertension treatment, systolic blood pressure, diastolic blood pressure, diabetes mellitus, valvular heart disease, prevalent myocardial infarction, and prevalent heart failure. CI indicates confidence interval; and HR, hazard ratio.

AF recurrence may have been insensitive to asymptomatic paroxysms of AF before the first-detected episode, thereby resulting in misclassification of the first-detected AF date and presence of secondary AF precipitants. Despite systematic routine Framingham Heart Study clinic visits and systematic review of all of the available intercurrent medical charts and diagnostics, in the absence of continuous cardiac rhythm monitoring we cannot exclude that subclinical AF may have predated the AF detected at the time of the secondary precipitant. Similarly, asymptomatic paroxysms of AF after the first episode[48] may have been undetected and, therefore, we may have underestimated the risk of AF recurrence. Increased vigilance may have led to differences in ECG ascertainment between individuals with and without secondary AF precipitants. However, the annual rate of ECGs during follow-up was similar between those with and without secondary precipitants in our analysis. Detected AF episodes include those that were represented in the medical chart and therefore were likely considered of clinical relevance at the time of the episode. We did not prospectively ascertain the duration, severity, or symptomatic nature of the first-detected AF event, which may potentially influence the likelihood of detected AF recurrence.

We had limited precision to assess for differences in risks of AF recurrence between specific secondary AF precipitants. Although we studied AF-related morbidity, we recognize that clinical events occurring after first-detected AF may not have been causally related to AF. Residual confounding may obscure associations between secondary precipitants and morbidity. We acknowledge that some potentially reversible precipitants were not represented in our analysis, including AF occurring in the context of electrolyte abnormalities, exposure to other medications, or other factors. It is not uncommon for older adults to have comorbidities, and it may be difficult to distinguish the etiology of AF in the setting of multiple comorbidities. The sample is composed of middle-age to older adults predominantly of European ancestry and our results therefore may not be generalizable to younger individuals or those of other racial and ethnic groups. Nevertheless, the age distribution of individuals with AF in our sample is representative of AF occurring in the US population.[49,50]

In conclusion, in our community-based sample of individuals with first-detected AF, most had recurrent AF at some point later in life. Nearly two-thirds of individuals with a seemingly reversible precipitant associated with a first-detected AF episode had recurrence of the arrhythmia. Individuals with AF associated with a potentially reversible cause had a lower risk of heart failure but similar risks of stroke and mortality over follow-up as compared with individuals without such precipitants. Increased vigilance appears warranted in patients with AF occurring in the context of secondary precipitants given the long-term likelihood of recurrence. Future studies may help determine whether increased arrhythmia surveillance or adherence to general AF management principles in patients with seemingly reversible AF precipitants will reduce morbidity.

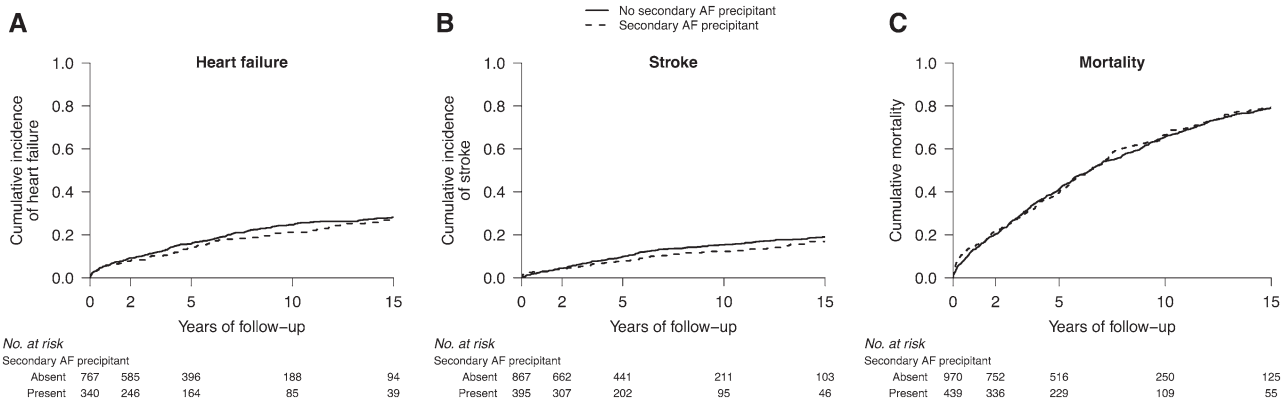

Figure 2. Risk of long-term morbidity by presence or absence of secondary atrial fibrillation precipitants. Panels display the cumulative risks of (**A**) incident heart failure, (**B**) incident stroke, and (**C**) mortality by secondary atrial fibrillation precipitants. In **A** and **B**, cumulative incidence estimates were adjusted for the competing risk of death.

Sources of Funding

This work was supported by National Institutes of Health grants K23HL114724 (to Dr Lubitz); N01-HC-25195, 6R01-NS17950, and 2R01HL092577 (to Drs Ellinor and Benjamin); 1R01 HL102214 (to Dr Benjamin), and R01HL104156 and K24HL105780 (to Dr Ellinor); a Doris Duke Charitable Foundation Clinical Scientist Development Award 2014105 (to Dr Lubitz); and an American Heart Association Established Investigator Award 13EIA14220013 (to Dr Ellinor). Dr Rienstra is supported by a grant from the Netherlands Organization for Scientific Research (Veni grant 016.136.055). Partial salary support is additionally provided by National Institutes of Health grants 1U01HL105268-01 and KL2RR031981 and Department of Defense grant W81XWH-12-FEST-IIA (to Dr McManus), as well as National Institutes of Health grant K01HL116768 (to Dr Walkey).

Disclosures

None.

References

1. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Kay GN, Le Huezey JY, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann LS, Smith SC Jr, Priori SG, Estes NA 3rd, Ezekowitz MD, Jackman WM, January CT, Lowe JE, Page RL, Slotwiner DJ, Stevenson WG, Tracy CM, Jacobs AK, Anderson JL, Albert N, Buller CE, Creager MA, Ettinger SM, Guyton RA, Halperin JL, Hochman JS, Kushner FG, Ohman EM, Stevenson WG, Tarkington LG, Yancy CW; American College of Cardiology Foundation/American Heart Association Task Force. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2011;123:e269–e367. doi: 10.1161/CIR.0b013e318214876d.
2. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW; ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2014;130:e199–e267. doi: 10.1161/CIR.0000000000000041.
3. Dawber TR, Meadors GF, Moore FE Jr. Epidemiological approaches to heart disease: the Framingham Study. *Am J Public Health Nations Health*. 1951;41:279–281.
4. Feinleib M, Kannel WB, Garrison RJ, McNamara PM, Castelli WP. The Framingham Offspring Study: design and preliminary data. *Prev Med*. 1975;4:518–525.
5. Wang TJ, Massaro JM, Levy D, Vasan RS, Wolf PA, D'Agostino RB, Larson MG, Kannel WB, Benjamin EJ. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA*. 2003;290:1049–1056. doi: 10.1001/jama.290.8.1049.
6. Schnabel RB, Rienstra M, Sullivan LM, Sun JX, Moser CB, Levy D, Pencina MJ, Fontes JD, Magnani JW, McManus DD, Lubitz SA, Tadros TM, Wang TJ, Ellinor PT, Vasan RS, Benjamin EJ. Risk assessment for incident heart failure in individuals with atrial fibrillation. *Eur J Heart Fail*. 2013;15:843–849. doi: 10.1093/eurjhf/hft041.
7. Lubitz SA, Yin X, Fontes JD, Magnani JW, Rienstra M, Pai M, Villalon ML, Vasan RS, Pencina MJ, Levy D, Larson MG, Ellinor PT, Benjamin EJ. Association between familial atrial fibrillation and risk of new-onset atrial fibrillation. *JAMA*. 2010;304:2263–2269. doi: 10.1001/jama.2010.1690.
8. Lubitz SA, Moser C, Sullivan L, Rienstra M, Fontes JD, Villalon ML, Pai M, McManus DD, Schnabel RB, Magnani JW, Yin X, Levy D, Pencina MJ, Larson MG, Ellinor PT, Benjamin EJ. Atrial fibrillation patterns and risks of subsequent stroke, heart failure, or death in the community. *J Am Heart Assoc*. 2013;2:e000126. doi: 10.1161/JAHA.113.000126.
9. Kannel WB, D'Agostino RB, Silbershatz H, Belanger AJ, Wilson PW, Levy D. Profile for estimating risk of heart failure. *Arch Intern Med*. 1999;159:1197–1204.
10. Gaynor JJ, Feuer EJ, Tan CC, Wu DH, Little CR, Straus DJ, Clarkson BD, Brennan MF. On the use of cause-specific failure and conditional failure probabilities: examples from clinical oncology data. *J Am Stat Assoc*. 1993;88:400–409.
11. Alonso A, Krijthe BP, Aspelund T, Stepas KA, Pencina MJ, Moser CB, Sinner MF, Sotoodehnia N, Fontes JD, Janssens AC, Kronmal RA, Magnani JW, Witteman JC, Chamberlain AM, Lubitz SA, Schnabel RB, Agarwal SK, McManus DD, Ellinor PT, Larson MG, Burke GL, Launer LJ, Hofman A, Levy D, Gottdiener JS, Kääb S, Couper D, Harris TB, Soliman EZ, Stricker BH, Gudnason V, Heckbert SR, Benjamin EJ. Simple risk model predicts incidence of atrial fibrillation in a racially and geographically diverse population: the CHARGE-AF consortium. *J Am Heart Assoc*. 2013;2:e000102. doi: 10.1161/JAHA.112.000102.
12. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB Sr, Newton-Cheh C, Yamamoto JF, Magnani JW, Tadros TM, Kannel WB, Wang TJ, Ellinor PT, Wolf PA, Vasan RS, Benjamin EJ. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet*. 2009;373:739–745. doi: 10.1016/S0140-6736(09)60443-8.
13. Gray RJ. A class of k-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat*. 1988;16:1141–1154.
14. Kerr CR, Humphries KH, Talajic M, Klein GJ, Connolly SJ, Green M, Boone J, Sheldon R, Dorian P, Newman D. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation: results from the Canadian Registry of Atrial Fibrillation. *Am Heart J*. 2005;149:489–496. doi: 10.1016/j.ahj.2004.09.053.
15. Lévy S, Maarek M, Coumel P, Guize L, Lekieffre J, Medvedowsky JL, Sebaoun A. Characterization of different subsets of atrial fibrillation in general practice in France: the ALFA study–the College of French Cardiologists. *Circulation*. 1999;99:3028–3035.
16. Nieuwlaat R, Capucci A, Camm AJ, Olsson SB, Andresen D, Davies DW, Cobbe S, Breithardt G, Le Heuzey JY, Prins MH, Lévy S, Crijns HJ; European Heart Survey Investigators. Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation. *Eur Heart J*. 2005;26:2422–2434. doi: 10.1093/eurheartj/ehi505.
17. Reynolds MR, Lavelle T, Essebag V, Cohen DJ, Zimetbaum P. Influence of age, sex, and atrial fibrillation recurrence on quality of life outcomes in a population of patients with new-onset atrial fibrillation: the Fibrillation Registry Assessing Costs, Therapies, Adverse Events and Lifestyle (FRACTAL) study. *Am Heart J*. 2006;152:1097–1103. doi: 10.1016/j.ahj.2006.08.011.
18. Nieuwlaat R, Prins MH, Le Heuzey JY, Vardas PE, Aliot E, Santini M, Cobbe SM, Widdershoven JW, Baur LH, Lévy S, Crijns HJ. Prognosis, disease progression, and treatment of atrial fibrillation patients during 1 year: follow-up of the Euro Heart Survey on atrial fibrillation. *Eur Heart J*. 2008;29:1181–1189. doi: 10.1093/eurheartj/ehn139.
19. Ruigómez A, Johansson S, Wallander MA, García Rodríguez LA. Predictors and prognosis of paroxysmal atrial fibrillation in general practice in the UK. *BMC Cardiovasc Disord*. 2005;5:20. doi: 10.1186/1471-2261-5-20.
20. Mills LC, Gow RM, Myers K, Kantoch MJ, Gross GJ, Fournier A, Sanatani S. Lone atrial fibrillation in the pediatric population. *Can J Cardiol*. 2013;29:1227–1233. doi: 10.1016/j.cjca.2013.06.014.
21. Takahashi N, Seki A, Imataka K, Fujii J. Clinical features of paroxysmal atrial fibrillation: an observation of 94 patients. *Jpn Heart J*. 1981;22:143–149.
22. Kopecky SL, Gersh BJ, McGoon MD, Whisnant JP, Holmes DR Jr, Ilstrup DM, Frye RL. The natural history of lone atrial fibrillation: a population-based study over three decades. *N Engl J Med*. 1987;317:669–674. doi: 10.1056/NEJM198709103171104.
23. Davidson E, Rotenberg Z, Weinberger I, Fuchs J, Agmon J. Diagnosis and characteristics of lone atrial fibrillation. *Chest*. 1989;95:1048–1050.
24. Rostagno C, Bacci F, Martelli M, Naldoni A, Bertini G, Gensini G. Clinical course of lone atrial fibrillation since first symptomatic arrhythmic episode. *Am J Cardiol*. 1995;76:837–839.
25. Scardi S, Mazzone C, Pandullo C, Goldstein D, Poletti A, Humar F. Lone atrial fibrillation: prognostic differences between paroxysmal and chronic forms after 10 years of follow-up. *Am Heart J*. 1999;137(4 pt 1):686–691.
26. Arriagada G, Berruezo A, Mont L, Tamborero D, Molina I, Coll-Vinent B, Vidal B, Sitges M, Berne P, Brugada J; GIRAFA (Grup Integrat de Recerca en Fibril.lació Auricular) Investigators. Predictors of arrhythmia recurrence in patients with lone atrial fibrillation. *Europace*. 2008;10:9–14. doi: 10.1093/europace/eum233.
27. Belluzzi F, Sernesi L, Preti P, Salinaro F, Fonte ML, Perlini S. Prevention of recurrent lone atrial fibrillation by the angiotensin-II converting enzyme inhibitor ramipril in normotensive patients. *J Am Coll Cardiol*. 2009;53:24–29. doi: 10.1016/j.jacc.2008.08.071.
28. Lubitz SA, Benjamin EJ, Ruskin JN, Fuster V, Ellinor PT. Challenges in the classification of atrial fibrillation. *Nat Rev Cardiol*. 2010;7:451–460. doi: 10.1038/nrcardio.2010.86.

29. Funk M, Richards SB, Desjardins J, Bebon C, Wilcox H. Incidence, timing, symptoms, and risk factors for atrial fibrillation after cardiac surgery. *Am J Crit Care*. 2003;12:424–434.
30. Lee SH, Kang DR, Uhm JS, Shim J, Sung JH, Kim JY, Pak HN, Lee MH, Joung B. New-onset atrial fibrillation predicts long-term newly developed atrial fibrillation after coronary artery bypass graft. *Am Heart J*. 2014;167:593–600.e591. doi: 10.1016/j.ahj.2013.12.010.
31. Kowey PR, Stebbins D, Igidbashian L, Goldman SM, Sutter FP, Rials SJ, Marinchak RA. Clinical outcome of patients who develop PAF after CABG surgery. *Pacing Clin Electrophysiol*. 2001;24:191–193.
32. Landymore RW, Howell F. Recurrent atrial arrhythmias following treatment for postoperative atrial fibrillation after coronary bypass operations. *Eur J Cardiothorac Surg*. 1991;5:436–439.
33. Izhar U, Ad N, Rudis E, Milgalter E, Korach A, Viola N, Levi E, Asraff G, Merin G, Elami A. When should we discontinue antiarrhythmic therapy for atrial fibrillation after coronary artery bypass grafting? A prospective randomized study. *J Thorac Cardiovasc Surg*. 2005;129:401–406. doi: 10.1016/j.jtcvs.2004.06.029.
34. Ariyarajah V, Malinski M, Khadem A, Harizi R, Wolfe K, Spodick DH. Relation of recurrence of atrial fibrillation after non-ST-elevation acute myocardial infarction to left atrial abnormality. *Am J Cardiol*. 2008;101:30–34. doi: 10.1016/j.amjcard.2007.07.044.
35. Walkey AJ, Hammill BG, Curtis LH, Benjamin EJ. Long-term outcomes following development of new-onset atrial fibrillation during sepsis. *Chest*. 2014;146:1187–1195. doi: 10.1378/chest.14-0003.
36. Siu CW, Jim MH, Zhang X, Chan YH, Pong V, Kwok J, Kung AW, Lau CP, Tse HF. Comparison of atrial fibrillation recurrence rates after successful electrical cardioversion in patients with hyperthyroidism-induced versus non-hyperthyroidism-induced persistent atrial fibrillation. *Am J Cardiol*. 2009;103:540–543. doi: 10.1016/j.amjcard.2008.10.019.
37. Nakazawa H, Lythall DA, Noh J, Ishikawa N, Sugino K, Ito K, Hardman SM. Is there a place for the late cardioversion of atrial fibrillation? A long-term follow-up study of patients with post-thyrotoxic atrial fibrillation. *Eur Heart J*. 2000;21:327–333. doi: 10.1053/euhj.1999.1956.
38. Koskinen P. A 4-year prospective follow-up study of the role of alcohol in recurrences of atrial fibrillation. *J Intern Med*. 1991;230:423–426.
39. Jabre P, Jouven X, Adnet F, Thabut G, Bielinski SJ, Weston SA, Roger VL. Atrial fibrillation and death after myocardial infarction: a community study. *Circulation*. 2011;123:2094–2100. doi: 10.1161/CIRCULATIONAHA.110.990192.
40. Walkey AJ, Wiener RS, Ghobrial JM, Curtis LH, Benjamin EJ. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. *JAMA*. 2011;306:2248–2254. doi: 10.1001/jama.2011.1615.
41. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, Barash PG, Hsu PH, Mangano DT; Investigators of the Ischemia Research and Education Foundation; Multicenter Study of Perioperative Ischemia Research Group. A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA*. 2004;291:1720–1729. doi: 10.1001/jama.291.14.1720.
42. Gialdini G, Nearing K, Bhave PD, Bonuccelli U, Iadecola C, Healey JS, Kamel H. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. *JAMA*. 2014;312:616–622. doi: 10.1001/jama.2014.9143.
43. Body SC, Collard CD, Shernan SK, Fox AA, Liu KY, Ritchie MD, Perry TE, Muehlschlegel JD, Aranki S, Donahue BS, Pretorius M, Estrada JC, Ellinor PT, Newton-Cheh C, Seidman CE, Seidman JG, Herman DS, Lichtner P, Meitinger T, Pfeufer A, Kääb S, Brown NJ, Roden DM, Darbar D. Variation in the 4q25 chromosomal locus predicts atrial fibrillation after coronary artery bypass graft surgery. *Circ Cardiovasc Genet*. 2009;2:499–506. doi: 10.1161/CIRCGENETICS.109.849075.
44. Wijffels MC, Kirchhof CJ, Dorland R, Allessie MA. Atrial fibrillation begets atrial fibrillation: a study in awake chronically instrumented goats. *Circulation*. 1995;92:1954–1968.
45. Epstein AE, Alexander JC, Gutterman DD, Maisel W, Wharton JM; American College of Chest Physicians. Anticoagulation: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005;128(2 suppl):24S–27S.
46. Virtanen R, Kryssi V, Vasankari T, Salminen M, Kivelä SL, Airaksinen KE. Self-detection of atrial fibrillation in an aged population: the LietoAF Study. *Eur J Prev Cardiol*. 2014;21:1437–1442. doi: 10.1177/2047487313494041.
47. Cooke G, Doust J, Sanders S. Is pulse palpation helpful in detecting atrial fibrillation? A systematic review. *J Fam Pract*. 2006;55:130–134.
48. Israel CW, Grönefeld G, Ehrlich JR, Li YG, Hohnloser SH. Long-term risk of recurrent atrial fibrillation as documented by an implantable monitoring device: implications for optimal patient care. *J Am Coll Cardiol*. 2004;43:47–52.
49. Naccarelli GV, Varker H, Lin J, Schulman KL. Increasing prevalence of atrial fibrillation and flutter in the United States. *Am J Cardiol*. 2009;104:1534–1539. doi: 10.1016/j.amjcard.2009.07.022.
50. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation: analysis and implications. *Arch Intern Med*. 1995;155:469–473.

CLINICAL PERSPECTIVE

There is widespread recognition that atrial fibrillation (AF) may recur episodically or be present in a sustained fashion after a first-detected episode, yet there exists a prevailing assumption that AF may occur as an isolated event without recurrence, particularly when an acute reversible or secondary precipitant is associated with the episode. We examined the risk of recurrent AF and related morbidity among 1409 community-dwelling individuals from the Framingham Heart Study with first-detected AF. Approximately one-third had a secondary precipitant of the arrhythmia, including surgery, infection, acute myocardial infarction, thyrotoxicosis, acute alcohol consumption, acute pericardial disease, pulmonary embolism, or other acute pulmonary disease. Despite being associated with a reduced risk of arrhythmia, nearly two-thirds of individuals with a secondary precipitant had recurrent AF within 15 years. Those with secondary precipitants, as compared with those without, had a 25% lower heart failure risk but similar stroke and mortality risks in follow-up. Our data suggest that AF occurring in acute care settings is an indicator of increased future AF risk. Furthermore, our observations suggest that AF episodes, irrespective of the precipitant, often serve as markers of elevated risk for long-term stroke and mortality. We submit that AF occurring in the context of a secondary precipitant should not be dismissed and that increased vigilance is warranted given the likelihood of arrhythmia recurrence. We advocate for systematic longitudinal examination of individuals with AF occurring in the context of a secondary precipitant and assessment of measures to reduce morbidity from this arrhythmia in such settings.